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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/965,529	LAL ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-93* is/are pending in the application.

4a) Of the above claim(s) *1-10,12-29 and 46-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 30-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01022002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

This application is a continuation of PCT Application Serial Number PCT/US00/22315, which claims the benefit of the filing date of provisional application 60/149,641 and 60/164,203.

Claims 94-129 were previously canceled.

Claims 1-93 are currently pending.

Election/Restrictions

1. Applicant's election without traverse of Group 76, claims 11 and 30-45, in the Paper filed October 20, 2003 is acknowledged.

2. Claims 1-10, 12-29 and 46-93 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the Paper filed October 20, 2003.

Accordingly, claims 11 and 30-45 are the subject of examination in the present Office Action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 11 and 30-45 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible asserted utility or a well-established utility.

The claims are most broadly drawn to antibodies directed to "a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 26, b) a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 26, c) a biologically active fragment of a polypeptide having the amino acid sequence of SEQ ID NO: 26, and d) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO: 26." Claims are

also drawn to the making of antibodies using the sequences [claims 36 and 39] and methods of diagnosis using the antibodies [claims 33 and 35].

The polypeptide of SEQ ID NO: 26 and naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 26 to which the claimed antibodies are directed are not supported by either a specific and substantial asserted utility or a well-established utility. The identity of SEQ ID NO: 26 is given in Table 2 of the instant specification only as that it is "homologous" to mouse transporter protein (MTP) and identification of some putative functional domains. The specification does not assert any specific and substantial utility of the polypeptide of SEQ ID NO: 26. A well established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Page 24, lines 7-16, and Table 1 of the instant specification disclose that the sequence of a nucleic acid sequence was determined from a number of fragment sequences that were assembled into a consensus sequence (SEQ ID NO: 63). The specification discloses at Table 4 that the source of the material for SEQ ID NO: 63 was a "library constructed using RNA from nasal polyp tissue removed from a 78-year-old Caucasian male during unilateral orchiectomy (with) indicated embryonal carcinoma." The sequence of the putative polypeptide sequence of SEQ ID NO: 26 was then deduced from this consensus sequence and compared to published database sequences, from which it was determined that the polypeptide of SEQ ID NO: 26 had "homology" to mouse transporter protein (MTP). The specification does not disclose the degree of "homology" that SEQ ID NO: 26 has to MTP, nor does the specification disclose a putative function of the putative SEQ ID NO: 26 polypeptide, only that it is one of several "membrane associated proteins" termed by specification as "MEMAPs." Identifying a DNA segment derived from cDNA fragments and determining a relationship of a deduced putative polypeptide product to a database polypeptide sequence based solely on primary polypeptide sequence does not endow the polypeptide with well established utility. There is no clear guidance from the specification regarding the "biological activity" of SEQ ID NO: 26 or that the polypeptide would have the same or similar biological properties as MTP because the "homology" of the computer deduced protein of SEQ ID NO: 26 is based solely upon computer alignment with known sequences of the cDNA sequences from which the amino acid sequence was deduced. There would be no predictability that this homology would render the biological activities of the putative polypeptide of SEQ ID NO: 26 and MTP similar because Applicant has not disclosed whether the biological activity of both polypeptides resides within the common region(s) or elsewhere within the sequence of the polypeptides, nor does the specification indicate whether the proteins share conserved active or binding sites. Brenner et al. (Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078; U on form PTO-

892), at page 6076, column 2, states that, "Fig. 2 shows one of the many pairs of proteins with very different structures that nonetheless have high levels of identity over considerable aligned regions. Despite the high identity, the raw and the statistical scores for such incorrect matches are typically not significant. The principal reasons percentage identity does so poorly seems to be that it ignores information about gaps and about the conservative or radical nature of residue substitutions. From the PDB90D-B analysis in Fig. 3, we learn that 30% identity is a reliable threshold for this database only for sequence alignments of at least 150 residues." Brenner therefore shows in Fig. 2 that reliance upon high identity alone in many pair wise comparisons is insufficient to relate information about structural and/or functional relatedness and in the analysis of Fig. 3 indicates that information which can be gleaned from sequence identity comparisons is database-specific, not general. The Brenner reference puts further emphasis on the need for structural relationships on page 6074, end of first column in the statement, "Since the discovery that the structures of hemoglobin and myoglobin are very similar though their sequences are not, it has been apparent that comparing structures is a more powerful (if less convenient) way to recognize distant evolutionary relationships than comparing sequences." Therefore, the Brenner reference teaches that sequence identity alone is insufficient to establish functional relationships between proteins, rather it must be used in concert with structural information to accurately establish relationships between proteins. The instant specification does not provide any information on the structural characteristics of SEQ ID NO: 26, only an assertion of 3 putative glycosylation sites, 5 putative phosphorylation sites, 4 putative transmembrane domains, a putative transmembrane 4 family signature, a putative lysosomal-associated transmembrane protein domain and homology with MTP (Table 2 for example), but this "homology" is based solely on the finding of sequence homology to MTP, and not actual structural determination. According to Brenner, sequence homology must be used in concert with structural information, rather than using one to guess the other. The instant specification does not provide any information about the structure of the predicted SEQ ID NO: 26 polypeptide, only sequence homology to the murine sequence MTP, and for this reason the specification provides insufficient information to enable the artisan to reasonably predict that SEQ ID NO: 26 is functionally related to MTP and therefore the specification does not teach the artisan a credible utility for SEQ ID NO: 26.

Because the characteristics of SEQ ID NO: 26 are based solely upon sequence identity of the protein with other previously known proteins and not based upon analysis of any actually-produced protein product, no biological activity has been established for SEQ ID NO: 26. As such, further research would be required to identify or reasonably confirm a "real world" context of use, for example, to identify any function of SEQ ID NO: 26 and conditions for which SEQ ID NO: 26 polypeptides, fragments and

"naturally occurring" 90% identical polypeptides would be of diagnostic or therapeutic significance. Accordingly, without a "real-world" use for the protein, antibodies specific therefore are equally not useful, as basic research such as studying the properties of the product of the polypeptide are not considered substantial and credible utility for the claimed invention. Therefore, the specification does not fairly disclose a substantial and credible utility for the antibody of the instant claims. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 10 and 30-45 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Additionally, even in view of a testable activity for those polypeptides that are "naturally-occurring" variants of SEQ ID NO: 26 comprising at least 90% identity, the specification still does not appear to provide sufficient guidance such that the skilled artisan is enabled to make and use an antibody to those polypeptides commensurate in scope with the instant claims. However, no such testable biological activity has been identified for the polypeptide of SEQ ID NO: 26, only that probes recognizing the nucleic acid encoding SEQ ID NO: 26 also identifies a nucleic acid species in several libraries of different tissue types and different disease conditions (Table 3 for example).

The specification discloses a single working example of a polypeptide that is naturally-occurring and has at least 90% identity to SEQ ID NO: 26; namely, the polypeptide of SEQ ID NO: 26. However, the genus of "naturally occurring" polypeptides which are 90% identical to the 226 amino acid residue sequence of SEQ ID NO: 26 encompasses as many as about 1.21×10^{46} different polypeptide molecules. Nevertheless, there is insufficient guidance in the specification as-filed to direct a person of skill in the art

as to how to make and use antibodies to a polypeptide comprising a "naturally-occurring" amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 26.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Applicant does not appear to provide sufficient guidance as to other sources of "naturally-occurring" polypeptides which are at least 90% identical to SEQ ID NO: 26. Even though the level of skill in the art for isolating "naturally-occurring" polypeptides encoded by nucleic acids related to the nucleic acid encoding SEQ ID NO: 26 may have been high with respect to the techniques employed, skill in the art does not render the existence of a "naturally-occurring" polypeptide predictable.

The presence of a single working example and the failure of the state of the art either at the time of filing or since to recognize other "naturally-occurring" polypeptides at least 90% identical to SEQ ID NO: 26 indicates that it was highly unpredictable that additional polypeptides meeting these limitation could be isolated, particularly based on the limited guidance provided in the specification as filed. Unlike the fact pattern of In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) where the presence of a hybridoma producing an antibody having the desired properties among the many hybridomas was predictable, in the instant case it is not predictable that other "naturally-occurring" polypeptides exist. Therefore, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue with respect to other "naturally-occurring" polypeptides other than SEQ ID NO: 26.

Consequently, a person of skill in the art is not enabled to make and use an antibody to a "naturally-occurring" polypeptide at least 90% identical to SEQ ID NO: 26 as encompassed by the full breadth of the claims as currently recited, irrespective of the particular form of the antibody (polyclonal, monoclonal, etc.).

5. Claims 11 and 30-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite as part of the invention an antibody which specifically binds a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 26."

A polypeptide comprising the amino acid sequence of SEQ ID NO: 26 is adequately described in the specification as-filed, thereby providing an adequate written description of an antibody which specifically binds the polypeptide of SEQ ID NO: 26 or immunogenic fragments thereof.

A polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 26" is a recitation of a genus of polypeptides for which Applicant has disclosed a single species: the polypeptide of SEQ ID NO: 26. The claim recites that the polypeptide to which the antibody binds is "naturally-occurring." The specification proposes that "variants" of MEMAP polypeptides in general include those having "at least about 80%, or alternatively at least about 90%, or even at least about 95% amino acid sequence identity to the MEMAP amino acid sequence, and which contains at least one functional or structural characteristic of MEMAP (page 25, lines 30-33 for example).

However, Applicant does not appear to have provided a description of which polypeptide sequences are "naturally-occurring", even among those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO: 26. Neither does Applicant appear to have provided a description of how the structure of the polypeptide of SEQ ID NO: 26 relates to the structure of other "naturally-occuring" polypeptides, even for those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO: 26. Thus neither the common attributes of the genus nor the identifying attributes of individual species other than SEQ ID NO: 26 appear to have been described.

One of skill in the art would conclude that Applicant was not in possession of the claimed genus of polypeptides comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 26." Since Applicant does not appear to have been in possession of the genus of polypeptides to which the instantly recited antibody specifically binds; Applicant in turn does not appear to be in possession of the genus of antibodies specifically binding these polypeptides.

Therefore, only an antibody to SEQ ID NO: 26 or immunogenic fragments thereof meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 11 and 30-45 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,448,230 to Ruben et al. (A on form PTO-892).

The '230 patent teaches peptide sequences of a protein related by sequence identity to mouse transporter protein (MTP; column 15, lines 36-51 in particular). It is noted from Table 2 of the instant specification, for example, that the polypeptide of SEQ ID NO: 26 is also related by sequence identity to MTP. The '230 patent teaches polypeptide sequences disclosed as SEQ ID NOs: 97 and 98 as fragments of the MTP related protein. The polypeptide of SEQ ID NO: 97 is 137 amino acids in length and is 99.3% identical to amino acid residues 9-145 of instant SEQ ID NO: 26. The polypeptide of SEQ ID NO: 98 is 87 amino acids in length and is 92.0% similar to amino acid residues 140-226 of instant SEQ ID NO: 26. The sequences of the '230 patent each comprise large contiguous stretches of sequence identity to the instant SEQ ID NO: 26. The '230 patent teaches antibodies to SEQ ID NOs: 97 and 98 that are useful as a diagnostic tool for identifying the protein (column 16, lines 16-25 in particular). The '230 patent teaches that antibodies to the peptides include Fab, $F(ab')_2$, single chain, chimeric and humanized antibodies. Given the high degree of identity between the polypeptides of the '230 patent and instant SEQ ID NO: 26, as well as the fact that they are all related by sequence identity to MTP, it is respectfully submitted that one skilled in the art would reasonably expect that the antibodies to the polypeptides of the '230 patent will also bind to instant SEQ ID NO: 26. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference between the materials, i.e., that the claims are directed to new materials and that such a difference would have been considered unexpected by one of ordinary skill in the art, that is, the claimed subject matter, if new, is unobvious. In the absence of evidence to the contrary, the burden is on the Applicant to prove that the claimed materials are different from those taught by the prior art and to establish patentable differences.

See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). The prior art teaching anticipates the claimed invention.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571)272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (571) 272-0841.Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
February 5, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER